1259591

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

December 10, 2004

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: *60/517,853*
FILING DATE: *November 06, 2003*
RELATED PCT APPLICATION NUMBER: *PCT/US04/37510*

Certified by

Jon W Dudas

Acting Under Secretary of Commerce
for Intellectual Property
and Acting Director of the U.S.
Patent and Trademark Office

Please type a plus sign (+) inside this box → [+]

PTO/SB/16 (5-03)
Approved for use through 4/30/2003. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Dudley Diego	Finch Restrepo	Boulder, CO Boulder, CO

☐ *Additional inventors are being named on th____ separately numbered sheets attached hereto*

TITLE OF THE INVENTION (280 characters max)

SHAPE MEMORY POLYMER COATED ELECTRODES

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

☐ Customer Number [ ] → *Place Customer Number Bar Code Label here*

OR *Type Customer Number here*

☒ Firm *or* Individual Name	Amy E. Rinaldo				
Address	KOHN & ASSOCIATES, PLLC				
Address	30500 Northwestern Hwy., Suite 410				
City	Farmington Hills	State	MI	ZIP	48334
Country	United States	Telephone	248-539-5050	Fax	248-539-5055

ENCLOSED APPLICATION PARTS *(check all that apply)*

☒ Specification *Number of Pages* 45 ☐ CD(s), Number [ ]

☒ Drawing(s) *Number of Sheets* 2 ☒ Other (specify) Acknowledgment Postcard

☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT *(check one)*

☒ Applicant claims small entity status. See 37 CFR 1.27.

☒ A check or money order is enclosed to cover the filing fees

☒ The Director is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 11-1449

☐ Payment by credit card. Form PTO-2038 is attached.

FILING FEE AMOUNT ($): $80.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☐ No.

☒ Yes, the name of the U.S. Government agency and the Government contract number are: NIG Grant DC00566

Respectfully submitted,

SIGNATURE [signature]

Date 11/06/03

TYPED or PRINTED NAME Amy E. Rinaldo

REGISTRATION NO. *(if appropriate)* 45,791

Docket Number: 7128.00004

TELEPHONE 248-539-5050

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PROVISIONAL APPLICATION COVER SHEET
Additional Page

PTO/SB/16 (8-00)
Approved for use through 10/31/2002. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Docket Number	7128.00004	Type a plus sign (+) inside this box →	+

INVENTOR(S)/APPLICANT(S)

Given Name (first and middle [if any])	Family or Surname	Residence (City and either State or Foreign Country)

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

"EXPRESS MAIL" Mailing Label Number EL 974 237 409 US

Date of Deposit 11-6-03

I hereby [illegible] deposited with the [illegible] Mail Post Office [illegible] under 37 CFR 1.10 on the [illegible] to the Assistant Commissioner for Patents, Washington, D.C. 20231

(Signature of person mailing paper or fee)

Number 2 of 2

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

PROVISIONAL PATENT APPLICATION

SHAPE MEMORY POLYMER COATED ELECTRODES

GRANT INFORMATION

NIH Grant DC00566

BACKGROUND OF THE INVENTION

1. FIELD OF THE INVENTION

Generally, the present invention relates to coated electrodes. More specifically, the present invention relates to electrodes that are able to ve inserted into the brain.

2. DESCRIPTION OF RELATED ART

Advances in detection and characterization of electroencephalographic (EEG) signals from the brain have allowed EEG monitoring to be useful in analysis of neurological and sleep disorders, and laboratory studies of vigilance. Recent advances have, for example, provided much information about the correlation between EEG signals and an individual's level of arousal, in a continuum from vigilance to drowsiness, and sleep onset. Shifts in EEG signals have been directly correlated with changes in performance, particularly during tasks that require sustained attention over prolonged periods of time. Devices for monitoring EEG signals are typically used in a laboratory environment or in a home for sleep studies, but are typically set up and operated by trained technicians. However, application of EEG monitoring to environments for study and monitoring of brain performance, such as for monitoring brain activity in the home, office, aircraft cockpit, and train or truck operations cabins, for example, has been severely hampered by cumbersome detection and recording equipment, and the need for the assistance of a

technician typically required to obtain high quality data.

In fitting EEG electrodes to the scalp of a subject being monitored, an EEG technician will typically first measure the distances between the nasium and the occipital bone, and between the mastoid processes, to identify the top center (Cz) of the head, and will then position all other electrodes relative to these landmarks to comply with the International 10/20 System that is well known in the art as the standard for positioning of EEG electrodes. The technician will then part the hair of the scalp of the subject at the intended electrode sites, clean the electrode sites to remove dirt, hair oil, and the like, and prepare the scalp to remove the top layer of dead skin, to ensure that scalp-electrode impedance values of less than 5 kΩ are obtained. The minimum level of impedance needed to minimize EEG artifact is dependent, in part, on the quality of the EEG amplifiers. Filtering certain environmental noises, such as 60 Hz interference, allows acceptable EEG signals to be acquired with impedance levels up to 100 kΩ. Other artifacts are magnified as the impedances increase unless the signal acquisition equipment has been designed to minimize these effects. For example, replacing a conventional EEG system that uses wires to transmit non-amplified EEG to the data acquisition/storage unit with a system that amplifies and digitizes the signals on the head will help to reduce movement artifacts. Maintaining sufficient downward pressure on an electrode with higher impedance values will minimize the contribution of artifacts resulting from the electrode sliding across hair or the scalp.

Conventionally, after preparation of the intended electrode sites on the scalp, electrodes are glued to the scalp with collodion, typically a viscous solution of pyroxilin, a commercially available nitrocellulose, in ether and alcohol, that is a particularly noxious preparation that can bond with the scalp and hair, to provide a stable scalp-electrode interface, until dissolved by a solvent such as acetone, or a non-acetone, oil based collodion remover.

A variety of hats, caps, helmets and headgear are known that have been developed to position EEG electrodes according to the International 10/20 System and provide a scalp-electrode interface without the use of an adhesive such as collodion. However, these types of devices still require technician assistance in the preparation of the electrode site, and are commonly uncomfortable and unacceptable for use during activities of work and daily living. One such sleep monitoring headgear utilizes a circumferential elastic headband to generate an electrode seating pressure for a single electrode located at the top center of the head of a subject. It has been found, however, that when such a circumferential elastic headband is utilized to seat multiple electrodes, the headband slides up and posteriorly on the forehead.

Such conventional hats, caps, helmets and headgear also typically make it difficult for a user to part the hair or abrade their scalp at the electrode site without assistance. For example, most of the electrode caps require a technician to abrade the scalp with a blunt tipped syringe and then inject conductive gel into the electrode embedded into the cap. Another conventional device requires the technician to lift or turn a disposable electrode on its side after a conductive gel on the electrode has made contact with the hair of the scalp, in order to part the hair at the intended area of the scalp for placement of the electrode. Several systems intended for use in the laboratory for non-ambulatory EEG monitoring dispense electrode gel to the electrode, but would make an EEG electrode locator headgear uncomfortably heavy and inconvenient for ambulatory use outside a laboratory environment. Another type of device utilizes sharp tipped metal points to penetrate the dead layer of skin. However, such sharp metal points can pose a medical danger due to the potential for infection, particularly with repeated abrasions, and the possibility of penetration of the skull if the device were to be struck accidentally during ambulatory activity, or other activities during daily living.

It would therefore be desirable to provide an EEG electrode and an EEG electrode locator assembly for use in combination with an EEG electrode locator headgear that allows the user to apply the electrodes at the electrode sites, permitting conventional scalp preparation techniques to be applied by the user without technical assistance. The present invention meets these needs.

DESCRIPTION OF THE DRAWINGS

Other advantages of the present invention are readily appreciated as the same becomes better understood by reference to the following detailed description when considered in connection with the accompanying drawings wherein:

Figure 1 is a schematic of the shape memory effect in polymers as defined by four critical temperatures;

Figures 2A and B are a photographs of sections of olfactory bulb with (Figure 2A) 25 µm gold microwire or (Figure 2B) embedded smp/gold electrode (150 X 300 µm); scale bar 300 µm, arrows point to gold microwire;

Figures 3A and B are photographs showing tissue response to implantation of 100 X 200 µm smp one week post-implantation; scale bar=200 µm;

Figures 4A and B are photographs showing tissue response to implantation of 100 X 200 µm smp after two weeks; scale bar=200 µm;

Figures 5A and B are photographs showing tissue response to a one week "slowly" (1 mm/ 40 minutes) inserted smp/gold wire implant (75 X 200 µm);

Figures 6A and B show Force measurement; Figure 6A shows a digital micrograph of an smp beam partially inserted into the olfactory bulb; and Figure 6B is a force-displacement graph;

Figures 7A-D are photographs showing two different designs (Figures 7A and B, and Figures 7C and D) for smp linear actuators with 25 μm embedded gold wire in the compressed state ((Figure 7A) and (Figure 7C)) and following thermal actuation ((Figure 7B) and (Figure 7D)); bars are 1 mm; and

Figures 8A and B are photographs showing the shape memory effect in polyglycolic acid (PGA); Figure 8A shows the shape after deformation at 120°C and Figure 8B shows the subsequent recovery above Tg; Bar is 1 mm.

DETAILED DESCRIPTION OF THE INVENTION

A polymer is a shape memory polymer if the original shape of the polymer is recovered by heating it above a shape recovering temperature (defined as the T_{trans} of a soft segment) even if the original molded shape of the polymer is destroyed mechanically at a lower temperature than the shape recovering temperature, or if the memorized shape is recoverable by application of another stimulus.

As used herein, the term "segment" refers to a block or sequence of polymer forming part of the shape memory polymer.

As used herein, the terms hard segment and soft segment are relative terms, relating to the T_{trans} of the segments. The hard segment(s) has a higher T_{trans} than the soft segment(s). The ratio by weight of the hard segment:soft segments is between about 5:95 and 95:5, preferably between 20:80 and

80:20.

As used herein, the term "biodegradable" refers to materials that are bioresorbable and/or degrade and/or break down by mechanical degradation upon interaction with a physiological environment into components that are metabolizable or excretable, over a period of time from minutes to three years, preferably less than one year, while maintaining the requisite structural integrity. As used herein in reference to polymers, the term "degrade" refers to cleavage of the polymer chain, such that the molecular weight stays approximately constant at the oligomer level and particles of polymer remain following degradation. The term "completely degrade" refers to cleavage of the polymer at the molecular level such that there is essentially complete mass loss. The term "degrade" as used herein includes "completely degrade" unless otherwise indicated.

Shape memory polymers can be thermoplastic, thermoset, interpenetrating networks, semi-interpenetrating networks, or mixed networks. Polymers can be a single polymer or a blend of polymers. Polymers can be linear, branched, thermoplastic elastomers with side chains or any kind of dendritic structural elements. Stimuli causing shape change can be temperature, ionic change, pH, light, electric field, magnetic field or ultrasound.

Thermoplastic shape memory materials can be shaped (e.g. molded) to a desired shape above the T_{trans} of the hard segment(s) and cooled to a temperature below the shape recovering temperature, where the polymer may undergo mechanical deformation, and strains are generated in the polymer. The original shape of the deformed polymers can be recovered by heating them to a temperature higher than their shape recovering temperature. Above this temperature, the strains in the polymer are relieved, allowing the polymer to return to its original shape. In contrast, thermoset

shape memory materials are shaped to a desired shape before the macromonomers used to form the thermoset polymers are polymerized. After the shape has been fixed, the macromonomers then are polymerized.

The polymer compositions are preferably compressible by at least one percent or expandable by at least five one of the original thickness at a temperature below the shape recovering temperature, with the deformation being fixed by application of a stimulus such as heat, light, ultrasound, magnetic fields or electric fields. In some embodiments, the materials show a ratio of recovery of 98% (compare to experimental examples).

When significant stress is applied, resulting in an enforced mechanical deformation at a temperature lower than the shape recovering temperature, strains are retained in the soft segments, or amorphous regions, and bulky shape change is kept even after the partial liberation of strain by the elasticity of the polymer. If the configuration of the molecular chains is disturbed by influencing the regulated arrangement of molecular chains at a temperature lower than the glass transition temperature, rearrangement of the molecular chains is assumed to occur through the increase of the volume size and the decrease of the free volume content. The original shape is recovered by the contraction of the hard segment aggregates by the elevation of the temperature according to rigid control of chain conformations and the shape of the polymer is restored to the memorized shape.

In addition to changes in state from a solid to liquid state (melting point or glass transition temperature), hard or soft segments can undergo ionic interactions involving polyelectrolyte segments or supramolecular effects based on highly organized hydrogen bonds. The SMP may undergo solid state to solid-state transitions (e.g. a change in morphology). Solid state to solid state transitions are well known to those of skill in the art, for example as in poly(styrene-block-butadiene).

An object formed using shape memory polymers can be prepared to control the direction of change during recovery. In other words, contraction and/or expansion can occur along one or more dimensional axes depending how the polymers are shaped and stressed. For example, in a SMP fiber, the change in shape can be limited to one dimension, such as along the length.

In another embodiment, the thermal and electrical conductivity of the SMP materials can be changed in response to changes in temperature.

The moisture permeability of the compositions can be varied, especially when the polymer is formed into a thin film (i.e., less than about 10 μm). Some polymer compositions, in their original shape, have a sufficient permeability such that molecules of water vapor can be transmitted through the polymer film, while water molecules are not large enough to penetrate the polymer film. The resulting materials have low moisture permeability at temperatures below room temperature and high moisture permeability at temperatures above room temperature.

The polymers incorporate "hard" and "soft" segments. The segments preferably are oligomers. As used herein, the term "oligomer" refers to a linear chain molecule having a molecular weight up to 15,000 Daltons. The polymers forming the segments are selected based on the desired glass transition temperature(s) (if at least one segment is amorphous) or the melting point(s) (if at least one segment is crystalline), which in turn is based on the desired applications, taking into consideration the environment of use. Preferably, the number average molecular weight of the polymer segment is greater than 400, and is preferably in the range of between 500 and 15,000.

The transition temperature at which the polymer abruptly becomes soft and deforms can be controlled by changing the monomer composition and

the kind of monomer, which enables one to adjust the shape memory effect at a desired temperature. The thermal properties of the polymers can be detected, for example, by dynamic mechanical thermoanalysis or differential scanning calorimetry (DSC) studies. In addition the melting point can be determined using a standard melting point apparatus.

The polymers can be thermoset or thermoplastic polymers, although thermoplastic polymers may be preferred due to their ease of molding. Thermosets, however, may be preferred in some applications, since they generally are softer than physically crosslinked polymer in their original shape at temperatures greater than T_{trans}.

Preferably, the degree of crystallinity of the polymer or polymeric block(s) is between 3 and 80%, more preferably between 3 and 60%. When the degree of crystallinity is greater than 80% while all soft segments are amorphous, the resulting polymer composition has poor shape memory characteristics.

The tensile modulus of the polymers below the T_{trans} is typically between 50 MPa and 2 GPa (gigapascals), whereas the tensile modulus of the polymers above the T_{trans} is typically between 1 and 500 MPa. Preferably, the ratio of elastic modulus above and below the T_{trans} is 20 or more. The higher the ratio, the better the shape memory of the resulting polymer composition.

The polymer segments can be natural or synthetic, although synthetic polymers are preferred. The polymer segments can be biodegradable or non-biodegradable, although biodegradable polymer compositions generally are preferred for in vivo medical applications. In general, these materials degrade by hydrolysis, by exposure to water or enzymes under physiological conditions, by surface erosion, by bulk erosion, or a combination thereof Non-

biodegradable polymers used for medical applications preferably do not include aromatic groups, other than those present in naturally occurring amino acids.

The polymers are selected based on the desired glass transition temperature(s) (if at least one segment is amorphous) or the melting point(s) (if at least one segment is crystalline), which in turn is based on the desired applications, taking into consideration the environment of use. Preferably, the number average molecular weight of the polymer block is greater than 400, and is preferably in the range of between 500 and 15,000.

The polymer may be in the form of a hydrogel (typically absorbing up to about 90% by weight of water), and can optionally be ionically crosslinked with multivalent ions or polymers. Ionic crosslinking between soft segments can be used to hold a structure, which, when deformed, can be reformed by breaking the ionic crosslinks between the soft segments. The polymer may also be in the form of a gel in solvents other than water or aqueous solutions. In these polymers, the temporary shape can be fixed by hydrophilic interactions between soft segments.

Representative natural polymer blocks or polymers include proteins such as zein, modified zein, casein, gelatin, gluten, serum albumin, and collagen, and polysaccharides such as alginate, celluloses, dextrans, pullulane, and polyhyaluronic acid, as well as chitin, poly(3-hydroxyalkanoate)s, especially poly(β-hydroxybutyrate), poly(3-hydroxyoctanoate) and poly(3-hydroxyfatty acids). Representative natural biodegradable polymer blocks or polymers include polysaccharides such as alginate, dextran, cellulose, collagen, and chemical derivatives thereof (substitutions, additions of chemical groups, for example, alkyl, alkylene, hydroxylations, oxidations, and other modifications routinely made by those skilled in the art), and proteins such as albumin, zein and copolymers and

blends thereof, alone or in combination with synthetic polymers.

Representative synthetic polymer blocks or polymers include polyphosphazenes, poly(vinyl alcohols), polyamides, polyester amides, poly(amino acid)s, synthetic poly(amino acids), polyanhydrides, polycarbonates, polyacrylates, polyalkylenes, polyacrylamides, polyalkylene glycols, polyalkylene oxides, polyalkylene terephthalates, polyortho esters, polyvinyl ethers, polyvinyl esters, polyvinyl halides, polyvinylpyrrolidone, polyesters, polylactides, polyglycolides, polysiloxanes, polyurethanes and copolymers thereof. Examples of suitable polyacrylates include poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate) and poly(octadecyl acrylate).

Synthetically modified natural polymers include cellulose derivatives such as alkyl celluloses, hydroxyalkyl celluloses, cellulose ethers, cellulose esters, nitrocelluloses, and chitosan. Examples of suitable cellulose derivatives include methyl cellulose, ethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, hydroxybutyl methyl cellulose, cellulose acetate, cellulose propionate, cellulose acetate butyrate, cellulose acetate phthalate, carboxymethyl cellulose, cellulose triacetate and cellulose sulfate sodium salt. These are collectively referred to herein as "celluloses".

Representative synthetic degradable polymer segments include polyhydroxy acids, such as polylactides, polyglycolides and copolymers thereof; poly(ethylene terephthalate); polyanhydrides, poly(hydroxybutyric acid); poly(hydroxyvaleric acid); poly[lactide-co-(s-caprolactone)]; poly[glycolide-co-(s-caprolactone)]; polycarbonates, poly(pseudo amino acids); poly(amino acids); poly(hydroxyalkanoate)s; polyanhydrides; polyortho esters; and blends and copolymers thereof. Polymers containing labile bonds,

such as polyanhydrides and polyesters, are well known for their hydrolytic reactivity. Their hydrolytic degradation rates can generally be altered by simple changes in the polymer backbone and their sequence structure.

Examples of non-biodegradable synthetic polymer segments include ethylene vinyl acetate, poly(meth)acrylic acid, polyamides, polyethylene, polypropylene, polystyrene, polyvinyl chloride, polyvinylphenol, and copolymers and mixtures thereof.

The polymers can be obtained from commercial sources such as Sigma Chemical Co., St. Louis, Mo.; Polysciences, Warrenton, Pa; Aldrich Chemical Co., Milwaukee, Wis.; Fluka, Ronkonkoma, N.Y.; and BioRad, Richmond, Calif. Alternatively, the polymers can be synthesized from monomers obtained from commercial sources, using standard techniques.

Hydrogels can be formed from polyethylene glycol, polyethylene oxide, polyvinyl alcohol, polyvinyl pyrrolidone, polyacrylates, poly (ethylene terephthalate), poly(vinyl acetate), and copolymers and blends thereof. Several polymeric blocks, for example, acrylic acid, are elastomeric only when the polymer is hydrated and hydrogels are formed. Other polymeric blocks, for example, methacrylic acid, are crystalline and capable of melting even when the polymers are not hydrated. Either type of polymeric block can be used, depending on the desired application and conditions of use.

For example, shape memory is observed for acrylic acid copolymers only in the hydrogel state, because the acrylic acid units are substantially hydrated and behave like a soft elastomer with a very low glass transition temperature. The dry polymers are not shape memory polymers. When dry, the acrylic acid units behave as a hard plastic even above the glass transition temperature and show no abrupt change in mechanical properties on heating. In contrast, copolymers including methyl acrylate polymeric blocks as the soft

segments show shape memory properties even when dry.

Certain polymers, for example, poly(ethylene oxide-co-propylene oxide) block copolymers (PLURONICS.TM., BASF) are soluble in water at temperatures lower than body temperature and become hydrogels at temperatures higher than body temperature. Incorporation of these polymers as blocks in shape memory polymers provides the shape memory polymers with the ability to response to changes in temperature in a manner totally opposite that of typical shape memory polymers. These materials recover their shape when cooled below their shape recovery temperature, rather than being heated above their shape recovery temperature. This effect is called inversed thermal shape memory effect. Shape memory polymer compositions including these polymer blocks are useful in various biomedical applications where the polymer can be inserted as a liquid, and cooled to recover an intended shape in situ. The inverse thermal shape memory effect can be obtained by incorporating two different blocks into a polymer that are miscible at temperatures lower than T_{misc} but are immiscible at higher temperatures. The phase separation at higher temperatures stabilizes the temporary shape.

Various polymers, such as polyacetylene and polypyrrole, are conducting polymers. These materials are particularly preferred for uses in which electrical conductance is important. Examples of these uses include tissue engineering and any biomedical application where cell growth is to be stimulated. These materials may find particular utility in the field of computer science, as they are able to absorb heat without increasing in temperature better than SMAs. Conducting shape memory polymers are useful in the field of tissue engineering to stimulate the growth of tissue, for example nerve tissue.

In a preferred embodiment, the shape memory polymer composition is able to hold more than one shape in memory. For example, the composition

can include a hard segment and at least two soft segments, wherein the T_{trans} of the hard segment is between -30 and 270°C, and is at least 10°C, and preferably 20°C, higher than the T_{trans} of one of the soft segments, and the T_{trans} of each subsequent soft segment is at least 10°C, and preferably 20°C, lower than the T_{trans} of the preceding soft segment. Optionally, one or more of the segments can be biodegradable or linked to another segment via a biodegradable linkage, such as ester-, amide-, anhydride-, carbonate-, or orthoester linkages.

The shape memory effect is based on the polymer morphology. With respect to thermoplastic elastomers, the original shape of an object is fixed by physical crosslinks caused by the hard segment. With respect to thermoset polymers, the soft segments are covalently crosslinked instead of having hard segments. The original shape is set by the crosslinking process.

In contrast to prior art segmented polyurethane SMPs, the segments of the compositions described herein need not be linear. The segments can be partially grafted or attached in dendremeric side groups.

The polymers can be in the form of linear diblock-, triblock-, tetrablock, or multiblock copolymers, branch or graft polymers, thermoplastic elastomers, which contain dendritic structures, and blends thereof. FIG. 3 illustrates some of the combinations of suitable classes of thermoplastic materials forming the hard and soft segments. The thermoplastic shape memory polymer composition also can be a blend of one or more homo- or co-polymer with one or more diblock-, triblock-, tetrablock, or multiblock copolymers, branch or graft polymers. These types of polymers are well known to those of skill in the art.

The polymers can be thermoset polymers. There are four different types of thermoset polymers that have shape memory capability. These

include polymer networks, semi-interpenetrating networks, interpenetrating networks, and mixed-interpenetrating networks.

A polymer network is prepared by covalently crosslinking macromonomers, i.e., polymers that contain polymerizable end groups such as carbon-carbon double bonds. The polymerization process can be induced by using light or heat sensitive initiators or by curing with ultraviolet light ("UV-light") without an initiator. Shape memory polymer networks are prepared by crosslinking one or more soft segments which correspond to one or more thermal transitions.

In an embodiment preferred for biomedical applications, the crosslinking is performed using a photocrosslinker and requires no chemical initiator. The photocrosslinker advantageously eliminates the need for initiator molecules, which may be toxic. FIG. 4 is a diagram of a reaction sequence for the synthesis of a preferred photocrosslinker, which produced an overall yield of about 65%.

Interpenetrating networks ("IPN") are defined as networks where two components are crosslinked, but not to each other. The original shape is determined by the network with the highest crosslink density and the highest mechanical strength. The material has at least two T_{trans} corresponding to the different soft segments of both networks.

A mixed IPN includes at least one physically crosslinked polymer network (a thermoplastic polymer) and at least one covalently crosslinked polymer network (a thermoset polymer) that cannot be separated by any physical methods. The original shape is set by the covalently crosslinked network. The temporary shapes correspond to the T_{trans} of the soft segments and the T_{trans} of the hard segment of the thermoplastic elastomer component.

A particularly preferred mixed interpenetrating network is prepared by polymerizing a reactive macromonomer in the presence of a thermoplastic polymer, for example, by the photopolymerization of carbon-carbon double bonds. In this embodiment, the ratio by weight of thermoset polymer to thermoplastic polymer is preferably between 5:95 and 95:5, more preferably, between 20:80 and 80:20.

Semi-interpenetrating networks ("semi-IPN") are defined as two independent components, where one component is a crosslinked polymer (a polymer network) and the other component is a non-crosslinked polymer (a homopolymer or copolymer), wherein the components cannot be separated by physical methods. The semi-IPN has at least one thermal transition corresponding to the soft segment(s) and the homo- or co-polymer components. The crosslinked polymer preferably constitutes between about 10 and 90% by weight of the semi-interpenetrating network composition.

The shape memory polymers can exist as physical mixtures of thermoplastic polymers. In one embodiment, a shape memory polymer composition can be prepared by interacting or blending two thermoplastic polymers. The polymers can be semicrystalline homopolymers, semicrystalline copolymers, thermoplastic elastomers with linear chains, thermoplastic elastomers with side chains or any kind of dendritic structural elements, and branched copolymers, and these can be blended in any combination thereof.

For example, a multiblock copolymer with a hard segment with a relatively high T_{trans} and a soft segment with a relatively low T_{trans} can be mixed or blended with a second multiblock copolymer with a hard segment with a relatively low T_{trans} and the same soft segment as that in the first multiblock copolymer. The soft segments in both multiblock copolymers are identical, so the polymers are miscible in each other when the soft segments are melted.

There are three transition temperatures in the resulting blend -that of the first hard segment, that of the second hard segment, and that of the soft segment. Accordingly, these materials are able to memorize two different shapes. The mechanical properties of these polymers can be adjusted by the changing the weight ratio of the two polymers.

Other kinds of blends of at least two multiblock copolymers, in which at least one of the segments is miscible with at least one of the segments of the other multiblock copolymers, can be prepared. If two different segments are miscible and build one domain together, then the thermal transition of this domain depends on the weight content of the two segments. The maximum number of memorized shapes results from the number of thermal transitions of the blend.

Shape memory blends may have better shape memory capabilities than the blend components alone. Shape memory blends are composed of at least one multiblock copolymer and at least one homo- or copolymer. Di-, tri-, or tetra-block copolymers should be suitable substitutes for a multiblock copolymer.

Shape memory blends are highly useful in industrial applications, since a broad range of mechanical, thermal, and shape memory capabilities can be obtained from only two or three basic polymers by blending them in different weight ratios. A twin-screw extruder is an example of standard process equipment that could be used to mix the components and process the blend.

In a preferred embodiment, the shape memory polymeric composition includes at least one hard segment and at least one soft segment or multiple soft segments that are covalently crosslinked, wherein at least two of the segments are linked via a functional group which is cleavable under application of light, changes in ionic concentration, changes in pH, electric

field, magnetic field, and/or ultrasound. In addition to changing shape in response to changes in temperature, the composition can change its shape in response to application of light, changes in ionic concentration, changes in pH, electric field, magnetic field and/or ultrasound. The temporary shape in these polymers is fixed by the covalent crosslinks.

Photoreversible reactions can be used to link soft segments together and hold the polymer in a temporary shape. The original shape of a material is set by the hard segment. Upon photochemical cleavage of these linkages, the material returns to its original shape. As these reactions are photoreversible, the bonds can be made and broken through several cycles. However, each time the bonds are broken, they need to be remade in order to memorize the shape. Examples of such functional groups capable of undergoing photoreversible reactions are cinnamon acid derivatives and cinnamylidene acid derivatives. Linking and cleavage can be induced by different wavelengths of UV-light. In addition cleavage can occur during a thermal treatment.

In another embodiment, the polymers can include side chains with chromophores, such as azo- groups, that absorb light. The chromophores also may be incorporated into the main chain. The hard and/or soft segments can also include double bonds that shift from cis to trans isomers when the chromophores absorb light. Light can therefore be used to isomerize the segment, which can dramatically affect the T_{trans} of the segment. The original shape of such polymers is set by the hard segment. The polymer then can be deformed into a temporary shape. The temporary shape can be fixed by curing the polymer with light to cause photoisomerization. In this way, the polymer is hindered from returning to its original shape, because the thermal transition temperature has been increased. Solid to solid phase transitions also may be induced in this manner.

Various functional groups are known to crosslink in the presence of certain ions or in response to changes in pH. For example, calcium ions are known to crosslink amine and alcohol groups, i.e., the amine groups on alginate can be crosslinked with calcium ions. Also, carboxylate and amine groups become charged species at certain pHs. When these species are charged, they can crosslink with ions of the opposite charge. The presence of groups that respond to changes in the concentration of an ionic species and/or to changes in pH on hard and/or soft segments results in reversible linkages between these segments. One can fix the shape of an object while crosslinking the segments. After the shape has been deformed, alteration of the ionic concentration or pH can result in cleavage of the ionic interactions that formed the crosslinks between the segments, thereby relieving the strain caused by the deformation and thus returning the object to its original shape. Because ionic bonds are made and broken in this process, it can only be performed once. The bonds, however, can be re-formed by altering the ionic concentration and/or pH, so the process can be repeated as desired.

Various moieties, such as chromophores with a large number of delocalized electrons, increase in temperature in response to pulses of applied electric or magnetic fields as a result of the increased electron flow caused by the fields. After the materials increase in temperature, they can undergo temperature induced shape memory in the same manner as if the materials were heated directly. These compositions are particularly useful in biomedical applications where the direct application of heat to an implanted material may be difficult, but the application of an applied magnetic or electric field would only affect those molecules with the chromophore, and not heat the surrounding tissue.

Various materials contain reactive functional groups that fragment in response to applied ultrasound. Examples of these groups are those that form stable radicals, such as nitroso and triphenylmethane groups. One can

fix the shape of an object while forming bonds between two or more soft segments, for example by using heat or light. After the shape is deformed, the application of ultrasound can break the bonds between the soft segments, and relieve the strain caused by the deformation. The object will then return to its original shape. Because covalent bonds are made and broken in this process, it can only be performed once.

The polymer used to form the segments in the SMPs described above are either commercially available or can be synthesized using routine chemistry. Those of skill in the art can readily prepare the polymers using known chemistry.

The compositions can be formed into a first shape under appropriate conditions, for example, at a temperature above the T_{trans} of the hard segments, and allowed to cool below the T_{trans} of the soft segment(s). Standard techniques are extrusion and injection molding. Optionally, the object can be re-formed into a second shape. Upon application of heat or other appropriate set of conditions, the object returns to original shape.

Thermoset polymers can be prepared by extruding the pre-polymerized material (macromonomers), and fixing the original shape at a temperature above the T_{trans} of the thermoset polymer, for example, by photocuring reactive groups on the monomer. The temporary shape is fixed by cooling the material below T_{trans} after deforming the material.

The crosslinking also can be performed in a solution of the macromonomers. The solvent is removed from the formed gel in a subsequent step.

Those compositions formed of thermoplastic polymers can be blown, extruded into sheets or shaped by injection molding, for example, to form

fibers. The compositions can also be shaped by other methods known to those of skill in the art for shaping solid objects, for example, laser ablation, micromachining, use of a hot wire, and by CAD/CAM (computer aided design/computer aided manufacture) processes. These processes are preferred for shaping thermoset polymers.

For several applications it is advantageous to go in small steps from a temporary shape to another temporary shape or the original shape. It is possible to go back and forth between shapes as needed, under the control of an operator.

Usually the T_{trans} of a shape memory polymer is sharp, so that the polymer will recover its original shape simply by heating the material only a few degrees Celsius. In an alternate embodiment, however, the shape memory polymer has a broad thermal transition, such that the original shape is fully recovered only when the polymer is heated higher than the upper limit of the thermal transition. A partial recovery will occur when heating at a temperature between the lower and the upper limits of the thermal transition. In this embodiment, the trigger is the temperature, and the effect is essentially independent of the time interval of heat application.

A certain amount of energy needs to be transferred to the shape memory polymer in order to recover a memorized shape. For the thermal shape memory effect, the amount of energy required to fully recover a memorized shape depends on the heat capacity of the material. For light sensitive materials, however, the amount of energy depends on the dosage of irradiation. In a preferred embodiment of a thermal shape memory effect, the polymer has a sharp thermal transition, which is triggered based on the duration the material is exposed to a temperature greater than Trans. Other factors affecting the transition include the mass or size of the material, and the temperature and heat transfer coefficient of the medium or environment in

contact with (and used to heat) the material. For example, the higher the temperature of the environment, the more quickly the memorized shape is recovered.

In case of the classical thermal shape memory effect, the entire polymer must be heated by application (and transfer) of heat energy from an external source in order to recover the original shape. In an alternate embodiment, the polymer is heated by energy sources other than temperature. Using these techniques it is possible not only to heat the whole shape memory device, but also selective parts of the shape memory device (another way of triggering and enhancing control to recover the original shape)

Polymers absorb light at different wavelengths, depending on their chemical structure. Polymers typically show strong absorption of radiation in the infrared (IR) and near-infrared (NIR) region. The strongest and most suitable absorption ranges for a particular polymer application can be identified using IR or NIR spectroscopy. Shape memory polymers also can show strong absorption in the ultraviolet (UV) region. The polymer can be cured with light including at least one of the specified frequencies in its spectra, such that the polymer will absorb the light energy and heat up.

The absorption characteristics of the shape memory polymer can be modified by the addition of a chromophor, which is a moiety, functional group, or molecule showing strong absorption in specific regions of the UV/visible/IR/NIR microwave spectrum. The chromophor can be covalently bound to the polymer, combined as a physical mixture with the polymer, or both.

In a preferred biomedical embodiment, light can be used to noninvasively control an implanted SMP device. For example, the implanted

polymer can be cured using specific external light sources that do not simultaneously heat tissue, serum, or other parts of the physiological environment surrounding the SMP implant. Such a light source (e.g., lamp) should emit one or more frequencies of light (e.g., near infrared, "NR") that are not absorbed by the physiological environment, but which are absorbed by the shape memory material. The use of NIR light is known in the diagnostics art.

In an alternate embodiment, the technique of interference is applied to control the light frequency applied to an implanted SMP. Interference provides three-dimensional (3-D) control of the region being cured, as the specific frequency of light being absorbed by the shape memory device is produced at a specified location by the interference of two or more beams crossed at the specified location. The sources of the beams are outside the body, and the frequencies of the beams generally are modulated radio frequencies selected to produce the desired application frequency from the resulting interference.

In an alternate embodiment, gas bubbles or bubble containing liquids, preferably fluorocarbons, are incorporated in the shape memory device. Using standard ultrasound technology, one can induce a cavitation effect in the gas/liquid to heat the SMP. Techniques for 3-D controlled application of ultrasound are known in the art of biomedical diagnostics.

It is also possible to effect energy transfers based on the interaction of the shape memory polymer and electromagnetic fields. Use of electromagnetic fields to induce heating or localized temperature changes are well known. In yet another embodiment, energy transfer is produced based on non-radiation effects, such as Foerster-Perrin energy transfer.

Shape memory polymer compositions can be prepared to have two original (permanent) shapes, i.e. a two-way shape memory effect. These

systems always consist of at least two components. The components are combined by layer techniques (similarly to bimetals) or are interpenetrating networks. By changing the temperature, the shape memory device changes its shape in the direction of permanent shape 1 or permanent shape 2. Each of the permanent shapes belongs to one component of the device. The shapes of the device always are in equilibrium between both shapes. The temperature dependence of the shape is caused by the fact that the mechanical properties of one component ("component A") are almost independent from the temperature in the temperature interval of interest. The mechanical properties of the other component ("component B") depend on the temperature. In one embodiment, component B becomes stronger at low temperatures compared to component A, while component A is stronger at high temperatures and determines the actual shape. A two-way memory device can be prepared by (a) setting the original shape of component A; (b) deforming the device into original shape of component B; and (c) fixing an original shape of component B while applying a stress to the component.

The recovery of the original shape of a shape memory polymer can be initiated by a hydrolytic degradation process. In a preferred embodiment, this feature is incorporated into a system including a thermoplastic polymer composed of a hard segment and at least one soft segment or a thermoset containing at least one soft segment (single component systems). In these polymers, two soft segments can be linked by a readily hydrolyzable bond. The term "readily hydrolyzable bond" is used herein to refer to groups having a hydrolysis rate that is greater than that for other functional groups in the polymer. The original shape of these polymers is determined by the hard segments (thermoplastic material) or the covalent crosslinks (thermoset). The temporary shape is fixed by the crosslinks between two soft segments after deforming the device. When the crosslinks between the soft segments are hydrolyzed, the original shape will be recovered. Readily hydrolyzable functional groups include activated ester bonds, such as glycolyl glycolate,

and anhydride bonds.

In another preferred embodiment, the polymer is a two-component system, in which at least one component is a covalent network, such as an IPN, a mixed-IPN, or a semi-IPN. The covalent network is an amorphous network having a very low T_{trans}. The covalent network determines the original shape of the system, and the second component deforms the system to fix the temporary shape. The second component is another network in the case of an IPN, a homo- or co-polymer in the case of a semi-IPN, and a thermoplastic elastomer in the case of a mixed-IPN. The first component (covalent network) hydrolyzes more slowly than the second component, such that the polymer recovers its original shape when the second component is degraded.

Shape memory polymer compositions, articles of manufacture thereof, and methods of preparation and use thereof are described. In a preferred embodiment, the shape memory polymer composition can hold more than one shape in memory. For example, the composition can include a hard segment and at least two soft segments. The T_{trans} of the hard segment is at least 10°C, and preferably 20 °C, higher than the T_{trans} of one of the soft segments, and the T_{trans} of each subsequent soft segment is at least 10°C, and preferably 20°C, lower than the T_{trans} of the preceding soft segment. A multiblock copolymer with a hard segment with a relatively high T_{trans} and a soft segment with a relatively low T_{trans} can be mixed or blended with a second multiblock copolymer with a hard segment with a relatively low T_{trans} and the same soft segment as that in the first multiblock copolymer. Since the soft segments in both multiblock copolymers are identical, the polymers are miscible in each other when the soft segments are melted. The resulting blend has three transition temperatures: one for the first hard segment, one for the second hard segment, and one for the soft segment. Accordingly, these materials are able to memorize two different shapes.

Any polymers that are crystalline or amorphous and that have a T_{trans} within the range defined herein can be used to form the hard and soft segments. The melting point or glass transition temperature (hereinafter, the T_{trans}) of the hard segment is at least 10°C, and preferably 20°C, higher than the T_{trans} of the soft segment. The T_{trans} of the hard segment is preferably between -30 and 270°C, and more preferably between 30 and 150°C The ratio by weight of the hard segment:soft segments is between about 5:95 and 95:5, preferably between 20:80 and 80:20.

In some embodiments, the shape memory polymers contain at least one physical crosslink (physical interaction of the hard segment) or contain covalent crosslinks instead of a hard segment. The shape memory polymers also can be interpenetrating networks or semi-interpenetrating networks. In addition to changes in state from a solid to liquid state (melting point or glass transition temperature), hard and soft segments may undergo solid-to-solid state transitions, and can undergo ionic interactions involving polyelectrolyte segments or supramolecular effects based on highly organized hydrogen bonds.

Articles of manufacture can be prepared from the shape memory polymer compositions, for example, by injection molding, blowing, extrusion, and laser ablation. To prepare an object having a shape in memory, the object can be formed at a temperature above the T_{trans} of the hard segment, and cooled to a temperature below the T_{trans} of the soft segment. If the object subsequently is formed into a second shape, the object can be returned to its original shape by heating the object above the T_{trans} of the soft segment and below the T_{trans} of the hard segment.

Articles of manufacture with two or more shapes in memory can be prepared by forming a polymer composition with a hard segment, a first soft

segment, and a second soft segment, where the first soft segment has a T_{trans} at least 10° C below that of the hard segment and at least 10° C above that of the second soft segment. After the composition is shaped at a temperature above the T_{trans} of the hard segment, it can be cooled to a temperature below that of the T_{trans} of the first soft segment and above that of the second soft segment and formed into a second shape. The composition can be formed into a third shape after it has been cooled below the T_{trans} of the second soft segment. The composition can be heated above the T_{trans} of the second soft segment to return the composition to the second shape. The composition can be heated above the T_{trans} of the first soft segment to return the composition to the first shape. The composition can also be heated above the T_{trans} of the hard segment, at which point the composition loses the memory of the first and second shapes and can be reshaped using the method described above.

Thermoset polymers can be prepared by pre-shaping macromonomers, for example, by extrusion, and fixing the original shape at a temperature above the T_{trans} of the thermoset polymer, for example, by photocuring reactive groups on the macromonomer. The original shape, however, can only be programmed one time.

In a preferred embodiment, the shape change occurs in response to a change in temperature. In another embodiment, however, the composition can change its shape in response to application of light, changes in ionic concentration and/or pH, electric field, magnetic field or ultrasound. For example, a SMP can include at least one hard segment and at least one soft segment, wherein at least two of the segments, preferably two soft segments, are linked to each other via a functional group that is cleavable under application of light, electric field, magnetic field or ultrasound. The temporary shape is fixed by crosslinking the linear polymers. By cleaving those links the original shape can be recovered. The stimuli for crosslinking and cleaving these bonds can be the same or different.

Shape memory polymer compositions, articles of manufacture thereof, and methods of preparation and use thereof are provided. The shape memory polymers can include at least one hard segment and at least one soft segment, or can include at least one kind of soft segment wherein at least one kind of the soft segments are crosslinked, without the presence of a hard segment. In a preferred embodiment, the polymers can hold two or more shapes in memory.

The present invention provides for an EEG electrode and an EEG electrode assembly for use in combination with an EEG electrode locator headgear for a user that allows the user to locate and apply the EEG electrodes accurately according to the International 10/20 System without technical assistance, to allow the acquisition of high quality EEG signals. The EEG electrode locator headgear is of the type that is portable and comfortable, allowing it to be worn by the user during daily activities as one would a cap or visor. The EEG locator headgear typically includes a plurality of locator straps connectable to one or more of the EEG electrode locators that form an electrode locator assembly with the EEG electrode for accurately positioning one or more of the EEG electrodes relative to the user's scalp, and for biasing the plurality of electrodes toward the user's scalp. Each EEG electrode is adapted to be received in and cooperate with a corresponding EEG electrode locator ring. Each EEG electrode includes a dispenser assembly adapted to dispense an electrically conductive gel through the user's hair onto the user's scalp. The dispenser assembly includes a base member for conducting EEG signals from the scalp of the user to a corresponding electrode locator ring for signal transmission to an EEG monitor.

The invention accordingly provides for an electroencephalograph (EEG) electrode locator assembly for use in combination with an EEG

electrode locator headgear for accurate positioning of the EEG electrode locator assembly on the scalp of a user. In a presently preferred embodiment, the EEG electrode assembly comprises an EEG electrode locator member adapted to be mounted to EEG electrode locator headgear; and an EEG electrode received in and removably electrically coupled to the EEG electrode locator headgear. The EEG electrode includes an electrically conductive base adapted to be in electrical communication with the scalp of a user for detecting EEG signals of the user. The EEG electrode and the electrically conductive base member typically may be made from a carbon and ABS composite plastic material with a silver/silver chloride (Ag/AgCl) coating. The EEG electrode locator member also typically may be made from a carbon and ABS composite plastic material with a Ag/AgCl coating, although the EEG electrode locator member may alternatively be made from another similar suitable electrically conductive material, such as stainless steel, for example. In one presently preferred aspect, the EEG electrode locator member comprises an electrically conductive ring having a central opening adapted to receive the EEG electrode. The EEG electrode locator member also preferably has a surface defining a plurality of slots for receiving and connection to one or more locator straps. The EEG electrode locator headgear preferably includes an electrical connector, and the EEG electrode locator member includes means for connecting the electrical connector to the EEG electrode locator member. In a presently preferred aspect, the means for connecting the electrical connector to the EEG electrode locator member comprises an electrical terminal connector aperture, and terminal connector screw.

In another presently preferred aspect, the EEG electrode is disposable. The EEG electrode base also preferably includes a housing defining a chamber for containing and dispensing an electrically conductive gel, and the housing of the EEG electrode base has a surface defining a lower gel dispenser opening for dispensing the electrically conductive gel. A porous

foam pad is also preferably attached to the EEG electrode base, by insertion of an upper annular flange of the foam pad into a corresponding annular groove of the electrode base. The porous foam pad provides padding for a comfortable scalp interface, absorbs the conductive gel to maintain a consistent volume of gel between the electrode base and scalp, and compresses with minimal downward pressure to minimize slide artifacts. The foam pad is easily disposable and replaceable, and is removably mounted to the EEG electrode base by a removable bottom connector ring. The bottom connector ring is removably received in a lower annular channel of the EEG electrode base that includes a plurality of inwardly projecting tabs that are received in a corresponding plurality of slots in the bottom connector ring. An annular groove or space is formed between the bottom connector ring and the housing of the EEG electrode base, with an edge portion of the porous foam pad removably received in the annular space, so that the porous foam pad can be removed from the EEG electrode base and replaced by another porous foam pad by removing and replacing the bottom connector ring.

The EEG electrode base housing also preferably includes an upper, outer radial flange, with a plurality of slots formed in the housing and the outer radial flange, and an outer radial groove connected to each of the slots in the housing, for receiving and mating with a corresponding plurality of inner mounting tabs on the electrode locator member, respectively, for removably coupling the EEG electrode to the EEG electrode locator member.

In a presently preferred aspect, the EEG electrode includes a flexible gel fill cap having an interior plunger portion for dispensing the conductive gel from the EEG electrode gel chamber. The flexible gel fill cap includes a lower outer radial flange mounted to the upper outer radial flange of the base, and the flexible gel fill cap preferably includes an upper gel fill port, through which the electrically conductive gel may be introduced into the EEG electrode gel chamber. In another presently preferred aspect, the flexible gel fill cap is

formed of a flexible, resilient material, so that by inversion of the gel cap by application of downward pressure on the gel cap to exert a pump action, the gel cap dispenses the conductive gel from the EEG electrode gel chamber. In another aspect, the EEG electrode includes an upper cap allowing the EEG electrode to be gripped for seating of the EEG electrode in the EEG electrode locator member, and in a presently preferred aspect, the upper cap has a surface defining opposing outer indentations for gripping and turning the upper cap for seating of the EEG electrode in the EEG electrode locator member.

The application of EEG monitoring to common daily environments for study and monitoring of brain performance during the normal course of daily activities has been severely hampered by cumbersome detection and recording equipment, and the need for the assistance of a technician to set up and monitor the acquisition of data in order to obtain high quality data. Simply parting the hair of the scalp and preparation of the desired portions of the scalp of a subject for proper placement of electrodes has commonly required the assistance of a technician. Particularly when disposable electrodes are to be applied by a user that are not bonded to the scalp of the user to provide an electrode-scalp interface, the proper preparation and placement of an electrode over hair can be critical for obtaining high quality signal data.

The invention is embodied in an electroencephalograph (EEG) electrode locator headgear that is portable and comfortable, and allows a user to locate and apply disposable EEG electrodes accurately according to the International 10/20 System without technical assistance, to allow the acquisition of high quality EEG signals.

The invention is further described in detail by reference to the following experimental examples. These examples are provided for the purpose of illustration only, and are not intended to be limiting unless otherwise specified. Thus, the invention should in no way be construed as being limited to the following examples, but rather, should be construed to encompass any and all variations which become evident as a result of the teaching provided herein.

EXAMPLES

Example 1:

Recent developments in neuronal ensemble recordings have greatly enhanced our understanding of the neural basis of behavior (Nicolelis and Ribeiro, 2002). The advent of novel methods for temporal control of gene expression in mice could potentially result in a revolution in the understanding of this relationship. However, in order to take full advantage of modern mouse genetics it is necessary to develop techniques to *routinely* measure the activity of neuronal ensembles in awake behaving mice (discussed in Nicolelis and Ribiero (2002)). Present techniques for recording ensemble neuronal activity are limited by the poor biocompatibility of materials and overall size of the implants.

In this application for a Bioengineering Research Grant (BRG, PA-02-011) we propose to develop and test the biocompatibility of novel electrode and packaging materials and develop a prototype chronic multi-electrode array brain implant with integrated electronics. A key hypothesis is that slow deployment (hours to days) of electrodes through thermal actuation of shape memory polymers (smp's) will greatly diminish the inflammatory astrocytic scar reaction that adversely affects long-term electrode performance. In addition, because design of biocompatible electrodes places specific constraints on electrical properties we incorporate parallel design of low

power implant electronics. Consistent with the guidelines for the BRG mechanism, our interdisciplinary approach relies on vigorous interplay between materials scientists, biomedical investigators and electrical engineers focused on producing a working brain implant optimized for long-term use in mice. This project is part of a larger effort to develop biological micro-probes using a combination of MEMS based fabrication technology (Micro Electrical Mechanical Systems) and cell biological approaches; a process we have termed CEMS, or Cellular Engineering Micro Systems. Utilizing sensors and actuators based in MEMS technology with microelectronics for control, signal processing and telemetry we envisage the fabrication of devices allowing micro scale movement of neuronal probes *in vivo*. CEMS implants would provide significant advantages over existing probes through long-term interaction with neurons in a "wire free" environment.

We will use the olfactory system in mice to test CEMS-based brain implants with integrated electronics for biocompatibility, reliability and signal to noise characteristics. Implants developed under this proposal will be used in experiments under grant DC00566 (D. Restrepo) to study the neural basis for olfactory behavior, and will be made available to other investigators, including our collaborator Dr. Miguel Nicolelis, who will use the implant in motor cortex.

Aim 1 To improve the biocompatibility of electrodes through the material engineering of smp composite electrodes that deploy gradually following implantation in the brain. Insertion of electrodes in brain tissue evokes an inflammatory astrocytic scar reaction that severely limits long-term electrode performance. We propose to test the hypothesis that both the rate of electrode insertion and the composition of electrode coatings are major factors contributing to the astrocytic scar. We propose that the use of low modulus, compliant materials capable of slow deployment *in situ* will minimize

adverse long-term tissue reactivity to electrode implantation. In order to deploy electrodes *in situ* at slow rates (hours to days), we will utilize thermally actuated composite electrodes fabricated from shape memory polymers (smps). Smps will be designed to deploy at body temperature at different rates, thereby allowing us to perform a thorough study of the effect of rate of deployment on the extent of astrocytic scar reaction. Composite smp electrodes will incorporate compliant gold conductors and will be attached to a base of lightweight polyimide. Different coatings of the tip of the electrode will be tested for biocompatibility, including bioresorbable coatings. The extent of the astrocytic scar reaction, necrosis, microgilal infiltration and apoptosis will be determined by immunohistochemistry. We will also quantify long-term electrode reliability by recording single unit responses at different times post-implantation. Changes in electrical parameters will be correlated to changes in the astrocytic scar reaction.

Aim 2. Design of low power miniaturized electronics and analysis of amplifier/probe interactions. We propose to design and develop electronics to perform the key functions of electrode site multiplexing, low-noise signal amplification, analog-to-digital conversion and digital data transmission. Our designs will emphasize the critical requirements for optimal signal-to-noise performance, ultra low-power operation and circuit area minimization necessary for incorporation into the CEMS implant prototype proposed in Aim 3. We will measure impedance characteristics of electrodes as well as responsiveness of electrodes to artificial spike-shaped voltage changes *in vitro*, and compare them to long-term changes in electrical properties due to encapsulation by astrocytes and chemical changes of the surface of the conductor *in vivo (measured in Aim 1)*. In addition, we will measure long-term changes in impedance of implanted electrodes *in vivo*. The electronics will be optimized to measure extracellular spike signals given constraints imposed by electrode characteristics, materials engineering and biocompatibility.

Aim 3. Fabrication and characterization of a prototype CEMS implant. We will incorporate the electronic implant developed in Aim 2 with the smp electrode assembly developed in Aim 3 and will link these to a surface module attached to the cranium that will serve the purpose of downloading data stored in the implant. The prototype CEMS implant, encapsulated in polyimide, will be inserted on the dorsal surface of the mouse olfactory bulb and will be tested for long-term performance 1 day to 12 weeks postimplantation. Performance will be assessed through long-term signal-to noise measurements of single units. We will also test the CEMS implant for biocompatibility by assessing the extent of tissue reactivity using immunohistochemistry.

Example 2:

Insertion of electrodes in neuronal or other tissue evokes an inflammatory reaction that severely limits long-term electrode performance. Here we disclose the use of shape memory polymer and bioresorbable polymer electrodes with incorporated microwire or nanowire conductors for minimal adverse tissue reactivity.

1. Use of shape memory polymers with embedded single or multiple microwire or nanowire conductors as electrodes for long term recording and stimulation in different tissues in the body including brain tissue. These smp electrodes would be capable of deployment at slow rates (minutes to days) post-implantation thereby minimizing adverse tissue reactivity.

2. Smp electrodes operate on the principle of using low modulus materials to better match the mechanical properties of tissue.

3. Deployment of smp electrodes at body temperature or higher with different

deployment characteristics (force and rate) that can be achieved through: choice of polymer, the degree of cross-linking and via the incorporation of a second phase of nanoparticulates or nanofibers.

4. Smp electrodes can deploy microwires and nanowires with improved electrical properties. This allows use of ductile metal microwires and nanowires that would buckle when inserted alone.

5. Slow deployment (minutes to days) of electrodes of other materials can be used to minimize tissue reactivity leading to improved long term performance.

6. Bioresorbable polymers with or without shape memory effects can be used to deploy microwire and nanowires electrodes in tissue leaving the wire suspended following resorption.

7. Deployment of bioresorbable electrodes with or without shape memory polymer effects at body temperature with different deployment characteristics (force and rate) can be achieved through: choice of polymer, the addition of a second phase (co-polymer or polymer blend), degree of cross-linking and via the incorporation of a second phase of nanoparticulates or nanofibers.

8. Biologicals or chemicals can be incorporated into the bioresorbable electrodes that would be released upon resorption to modify tissue reactivity, promote or inhibit cell and extracellular matrix adhesion or to serve as a biological tracer of insertion site. Timing of release can be tailored by changing the properties of the bioresorbable polymer.

9. Biologicals or chemicals can be incorporated on the surface of shape memory polymer electrodes that would be released or directly interact with

surrounding tissue to modify tissue reactivity and promote or inhibit cell and extracellular matrix adhesion.

10. Microwires and nanowires can be coated with alumina using atomic layer deposition in order to insulate the surface of the electrode, except at the tip.

11. The surface morphology can be modified in the nano and micro scale to modify the interaction of the electrodes with surrounding tissue.

1. NOVELTY.

Shape memory polymers. Shape memory polymers (smp's) and smp composites (Gall et al., 2002;Tobushi et al., 1992) are an attractive compliant material that has not been proposed for use in electrodes. The thermo-mechanical response of shape memory polymers is shown schematically in Fig. 2, as defined by four critical temperatures. The glass transition temperature, T_g, is the reference point for thermo-mechanical deformation and recovery. An advantage of smp's is that T_g can be easily varied over a temperature range of several hundred degrees by control of chemistry or degree of cross-linking. The deformation temperature, T_d, is the temperature at which the polymer is deformed into its temporary shape (Fig. 2). The initial deformation at T_d can occur above or well below T_g depending on the desired recovery response (Gall et al., 2002). The storage temperature, T_s, is below T_d and constitutes the temperature at which the temporary shape is stable over time. After deformation at T_d, the material is typically cooled to T_s with varying degrees of strain/stress constraint ranging from no constraint to full constraint (Fig. 2). The recovery temperature, T_r, represents the temperature range at which the material recovers its original shape during heating. Recovery can be accomplished isothermally by heating to a fixed T_r and then holding, or by continued heating up to and past T_r (Gall et al., 2002;Liu et al., 2003).

Because these polymers can be fabricated to the micron scale using photolithographic techniques this allows for reproducible fabrication of compliant electrodes. Further, by adding different materials it is possible to control the actuation force and rate of deployment (minutes to hours), making it possible to deploy the electrode in a minimally invasive manner. Although not intrinsically conductive, smp's can be fabricated with microwire inclusions or can have evaporated conductive wires patterned on the surface using electron beam evaporated gold.

Electrodes elicit an inflammatory response analogous to the response in brain stab wound. One of the major limitations of present technology in implantable electrodes is poor long-term biocompatibility and degradation of electrical reliability. Ideally, an implanted electrode should not impact the surrounding cells thereby providing for stable long-term recording of extracellular field potentials from neighboring neurons. Electrode materials should be compliant thereby minimizing differential movement of the electrode with respect to brain tissue. However, immediately upon insertion of microwire or silicon micromachined electrodes, there is tissue inflammation and necrotic cell death. Interestingly, the quality of recording from chronic microwire electrodes *increases* in the first few days of recording, likely due to decrease in tissue inflammation and edema. However, a longer-term reactive astrocytic reaction ensues that result in physical blockage of the electrode by a surrounding sheath of reactive astrocytes. This "astrocytic scar" as well as corrosion of the electrode surface contribute to progressive signal degradation (Maynard et al., 2000;Nadol, Jr. et al., 2001;Rousche et al., 2001;Rousche and Normann, 1998;Turner et al., 1999;Williams et al., 1999). Two components of the astrocytic tissue reaction, short-term and long term, have been described. It has been postulated that electrode geometry and device size influence only the short term reaction. The implication being that the long term reactions are exclusively due to material biocompatibility

(Szarowski et al., 2003). While this conclusion is likely correct for the conditions tested in the Szarowski manuscript, the range of electrode cross-sections tested was limited, and bioresorbable materials were not used in that study. In addition, a causal relationship between the long-term and short-term reactions cannot be discarded in that study because the short-term reaction was significant under all conditions tested in that study.

The causal relationship between the initial necrosis and subsequent inflammation and astrocytic scar is not well understood for electrode insertion. Brain stab wound, a process with significant parallels to electrode insertion injury, is much better understood. Studies of brain stab injury indicate that the insertion of a sharp foreign object into brain tissue elicits blood spillage and cell necrosis thereby causing large increases in the concentration of glutamate, a molecule that is normally used by the central nervous system as a neurotransmitter, but becomes exitotoxic at high concentration. Glutamate causes exitotoxicity in neurons promoting further necrosis and triggering an inflammatory reaction with recruitment of microglia, the immune cells of the nervous system. Within a few days signaling molecules released by the microglia, presumably cytokines, elicit formation of an "astrocytic scar" made up of reactive astrocytes surrounding the wound. In parallel, and perhaps mediated through microglia activation, there is a slower development of apoptosis (programmed cell death) in a period of days to weeks (Beattie et al., 2000;Citron et al., 2000;Eldadah and Faden, 2000;Giulian et al., 1989;Knoblach et al., 2002;Krum et al., 2002;Roitbak and Sykova, 1999;Snider et al., 1999;Turner et al., 1999;Tzeng and Wu, 1999).

Several aspects of tissue response to stab wound are problematic for long-term measurement with microelectrode arrays. Astrocytic scars are an electrical barrier between the electrodes and the neighboring neurons, resulting in decreased signal-to-noise ratio. In addition, given that there is little adult neurogenesis, neuronal apoptosis causes irreversible loss of the source

of electrical signals. It is therefore extremely important to decrease the magnitude of the inflammatory reaction to electrode insertion. A major hypothesis in stab brain injury is that the adverse reaction to the stab is triggered by large increases in glutamate concentration that cannot be handled by normal glutamate homeostasis mechanisms. Since a major source of glutamate is spillage from injured cells and damaged blood vessels in the electrode insertion path, we propose to test the hypothesis that slow rates of insertion (hours to days) will result in a smaller increase in glutamate concentration and in a diminished tissue reaction. This will in turn lead to improved long term performance of electrodes.

Bioresorbable polymers. Polyesters based on polylactic acid (PLA), polyglycolic acid (PGA) and their copolymers are the most commonly used materials for their bioresorbable characteristics. They are biocompatible and FDA approved (for a particular form of synthesis)(Vert et al., 1998). While the mechanisms of hydrolytic degradation are complex, the rate of degradation ranging from weeks to months can be controlled either through composition as in forming polymer blends or through the addition of initiators. The breakdown products of PLA and PGA are L- or D- lactic and glycolic acid respectively (Ignatius and Claes, 1996), all of which are normally present in the human body. These are typically metabolized by cells surrounding the material by means of the citrate cycle yielding carbon dioxide which is finally eliminated by respiration (Brandt et al., 1984). The combination of bioresorbability and shape memory effect has been studied by (Lendlein and Langer, 2002) based on a linear, phase-segregated multiblock copolymer as the structural concept with successful results in terms of cyclic thermomechanical properties showing deployment at 37°C and with linear mass loss of around 50% in 300 days. There appears to be no literature on the basic shape memory properties of PGA, PLA or co-polymers.

Typically, electrodes are inserted quickly into tissue (in the order of minutes).

Indeed, the University of Utah group has proposed that inserting electrodes quickly by shooting them with a pneumatic gun would be advantageous. If slow deployment were performed by using a micromanipulator, patients would have to be kept under anesthesia for long times thereby increasing the risk of death. The use of shape memory polymers to slowly deploy electrodes is not obvious.

-Individuals attempting to understand the neural basis of behavior can use the present invention.

-Neurosurgeons interested in curing mental disease, cognitive and physical disabilities

-Physicians interested in recording from any tissue or organ for physiological examination of body functions.

Current electrodes are made from microwires or silicon micromachined materials. These materials elicit adverse tissue reactivity.

Embedded smp electrodes can be sectioned for histological processing in olfactory bulb *in situ*. Complete analysis of the tissue response to electrode insertion would ideally include the histological examination of the brain with the electrode *in situ*. Most studies remove the implant prior to sectioning of the tissue. Alternatively, some investigators perform the laborious task of attempting to section parallel to implants in order not to disrupt the tissue when the sectioning knife contacts the implant material. We were interested in determining whether it would be possible to section fine wires (<25 μm) or embedded smp electrodes without disrupting the tissue.

Individual wires (25 μm diameter) or embedded smp electrodes were inserted into the olfactory bulbs of mice immediately after euthanasia. The bulbs were then removed, immersion fixed and prepared for cryosectioning

(18 μm sections). It was not possible to section any of the wires tested (stainless steel, W, W/Ir, Au, Ag, Ni) without some damage to the tissue. However, the softer metals (e.g. Au and Ag, Fig 3(a)) sectioned, albeit with some tearing. Interestingly, gold and silver wires that were embedded in smp were routinely cut without causing tissue disruption (Fig. 3(b)). Generally, the smp remained attached to the tissue section after processing. The ability for the embedded smp's to remain adhered to the tissue during processing increases the ability to properly analyze the tissue response due to implantation of novel electrode materials. Notice that in these preliminary experiments the smp electrodes are large. In Aim 1 we plan to decrease the size of smp electrodes.

Initial characterization of biocompatibility of smp electrodes. Fig. 4 shows a cross section of an olfactory bulb one week after implantation with an smp beam. The section was reacted with an antibody to GFAP, a selective marker of astrocytes, and counter stained with hemotaxolin and eosin. The implant caused gross disruption of tissue histology including a massive infiltration of astrocytes around it. Additionally, we detected slight increases in the number of microglia and apoptotic cells (not shown). Interestingly, the extent of astrocytic scaring appears less than that reported for Si micromachined electrodes (Szarowski et al., 2003). Further, examination of an olfactory bulb two weeks after implantation (Fig. 5) shows less astrocytosis compared to one week post-implantation (Fig. 4). A decrease in astrocytosis with time was not evident in studies with Si micromachined electrodes (Szarowski et al., 2003), and may indicate better biocompatibility for smp implant materials.

Slow rate of insertion may decrease tissue reactivity. In order to explore the possibility that slow rates of implant insertion might cause decreased tissue reactivity, we compared the astrocytic scaring resulting one week after insertion of a rapidly inserted smp beam (~1 mm/sec, Fig. 4) and an

embedded gold microwire smp electrode inserted more slowly (1 mm/40 min, Fig. 6) using an electronically controlled micromanipulator. Remarkably, the slowly deployed embedded smp electrode caused very little astrocytic scarring. This result supports our hypothesis that slow insertion of implants will reduce the extent of damage to the tissue. It is compelling to hypothesize that thermally actuated smp electrodes that deploy over the course of many hours or days may actually induce even less tissue damage.

Forces for insertion of smp electrodes into mouse olfactory bulb are well below forces generated by thermal actuation of smp's. Fig. 7(a) shows the tip of an smp electrode without an embedded microwire partially inserted into a mouse olfactory bulb. Force of insertion was measured at NIST on the basis of Hooke's law using a piezoelectric actuator specifically designed to measure force in the 5 μN-100 mN range. The smp materials were capable of providing sufficient stiffness to avoid kinking or buckling of the electrode as they were inserted into the mouse olfactory bulb even without the presence of the microwire for added rigidity. Fig. 7(b) shows the force of insertion as a function of distance. The magnitude of the insertion forces measured in mouse olfactory bulb (ca 40 μN) are consistent (after scaling for probe size) with forces measured in pig brain (ca 100 mN)(Miller et al., 2000). Forces measured in olfactory bulb are several orders of magnitude below the mN forces that can be generated by smp materials (Gall et al., 2002). This indicates that smp materials should be capable of generating enough force for deployment in the brain following surgical implantation.

Thermal deployment of smp linear actuator with embedded electrodes. Fig. 8 shows two designs for linear actuators, one with an embedded 25 μm gold conductor. In these initial tests we were able to obtain linear deployments of 280 μm (Fig. 8(b)) and 170 μm (Fig. 8(d)). With refinement we expect to be able to obtain deployment of 500 μm.

Shape memory effect of bioresorbable PGA polymers. An initial attempt has been made to evaluate the shape memory effect of bioresorbable PGA. Heating the polymer from the solid state and applying a compressive force at 120°C prior to cooling to room temperature shows this polymer retains the deformed pattern. Although the shape memory effect is weaker than that exhibited by epoxy based materials, initial measurements show that re-heating the PGA polymer results in recovery (Fig. 9). These results are extremely encouraging since increasing the Tg by way of adding a second phase (e.g. blending with Poly Lactic Acid (PLA)) or cross-linking of the PGA polymer should have a significant impact on the force of recovery.

Figure 1 is a schematic of the shape memory effect in polymers as defined by four critical temperatures. The value of T_p is a material property that can be altered depending on the application. Typically, T_s is always less than T_g, while T_d may be above or below T_g, depending on the desired recovery response. The value of T_r will depend on both T_d and T_g;

Fig. 2. Sections of olfactory bulb with (a) 25 µm gold microwire or (b) embedded smp/gold electrode (150 X 300 µm). Implant in (b) appears somewhat larger than the actual dimensions due to the angle of sectioning. Scale bar 300 µm. Arrows point to gold microwire;

Fig. 3. Tissue response to implantation of 100 X 200 µm smp one week post-implantation. Implanted olfactory bulb (a) showed a large infiltration of astrocytes stained for GFAP (brown) around the implant compared to the contralateral bulb (b). Scale bar=200 µm;

Fig. 4. Tissue response to implantation of 100 X 200 µm smp after two weeks. The astrocytic scar around the implant in (a) is smaller and less dense than that for a one week implant (Fig. 4). Note that the shape and size of the implant are odd due to the severe misalignment of the bulb before sectioning.

(b) Section through the control contralateral bulb. Scale bar=200 μm;

Fig. 5. Tissue response to a one week "slowly" (1 mm/ 40 minutes) inserted smp/gold wire implant (75 X 200 μm). The implanted bulb (a) showed an increase in astrocytes around the implant when compared to the control bulb (b), but the extent of the astrocytic scar was less then that seen for rapidly inserted implants (Figs.4,5). Notice that the presence of astrocytes in midline is a normal feature of the bulb;

Fig. 6. Force measurement. Top Digital micrograph of an smp beam partially inserted into the olfactory bulb (on left). Bottom: Force-displacement graph. Taper was entirely covered at 400 μm, where the slope relates to the friction of insertion reaching a maximum of 0.1 mN;

Fig. 7. Two different designs (a and b, and c and d) for smp linear actuators with 25 μm embedded gold wire in the compressed state ((a) and (c)) and following thermal actuation ((b) and (d)). Bars are 1 mm; and

Fig. 8. Shape memory effect in poly glycolic acid (PGA). (a) Shape after deformation at 120°C and (b) subsequent recovery above Tg. Bar is 1 mm.

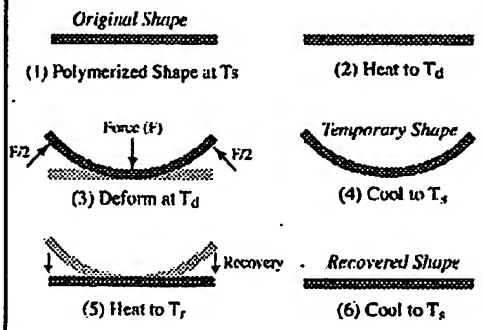
Throughout this application, various publications, including United States patents, are referenced by author and year and patents by number. Full citations for the publications are listed below. The disclosures of these publications and patents in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

The invention has been described in an illustrative manner, and it is to be understood that the terminology which has been used is intended to be in

the nature of words of description rather than of limitation.

Obviously, many modifications and variations of the present invention are possible in light of the above teachings. It is, therefore, to be understood that within the scope of the appended claims, the invention can be practiced otherwise than as specifically described.

Fig. 1. Schematic of the shape memory effect in polymers as defined by four critical temperatures. The value of T_g is a material property that can be altered depending on the application. Typically, T_s is always less than T_g, while T_d may be above or below T_g, depending on the desired recovery response. The value of T_r will depend on both T_d and T_g.



T_s = Storage Temperature
T_d = Deformation Temperature
T_r = Recovery Temperature
T_g = Glass Transition Temperature

Fig. 2. Sections of olfactory bulb with (a) 25 µm gold microwire or (b) embedded smp/gold electrode (150 X 300 µm). Implant in (b) appears somewhat larger than the actual dimensions due to the angle of sectioning. Scale bar 300 um. Arrows point to gold microwire.

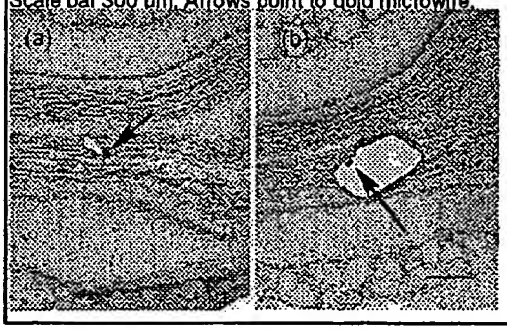


Fig. 3. Tissue response to implantation of 100 X 200 •m smp one week post-implantation. Implanted olfactory bulb (a) showed a large infiltration of astrocytes stained for GFAP (brown) around the implant compared to the contralateral bulb (b). Scale bar=200 •m.

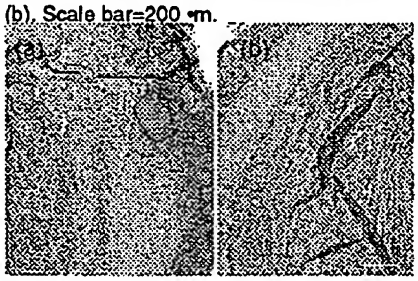


Fig. 4. Tissue response to implantation of 100 X 200 µm smp after two weeks. The astrocytic scar around the implant in (a) is smaller and less dense than that for a one week implant (Fig. 4). Note that the shape and size of the implant are odd due to the severe misalignment of the bulb before sectioning. (b) Section through the control contralateral bulb. Scale bar=200 µm.

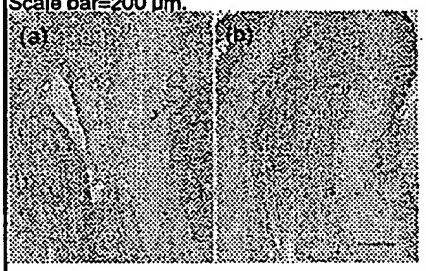


Fig. 5. Tissue response to a one week "slowly" (1 mm/ 40 minutes) inserted smp/gold wire implant (75 X 200 µm). The implanted bulb (a) showed an increase in astrocytes around the implant when compared to the control bulb (b), but the extent of the astrocytic scar was less then that seen for rapidly inserted implants (Figs.4,5). Notice that the presence of astrocytes in midline is a normal feature of the bulb.

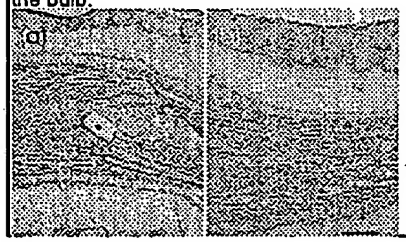


Fig. 6. Force measurement. Top Digital micrograph of an smp beam partially inserted into the olfactory bulb (on left). Bottom: Force-displacement graph. Taper was entirely covered at 400 µm, where the slope relates to the friction of insertion reaching a maximum of 0.1 mN.

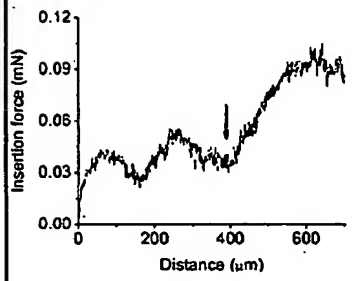


Fig. 7. Two different designs (a and b, and c and d) for smp linear actuators with 25 µm embedded gold wire in the compressed state ((a) and (c)) and following thermal actuation ((b) and (d)). Bars are 1 mm.

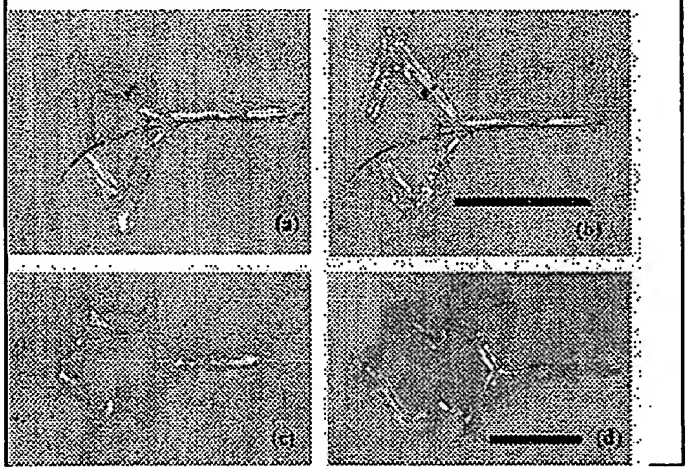
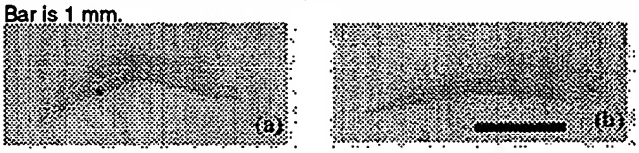


Fig. 8. Shape memory effect in poly glycolic acid (PGA). (a) Shape after deformation at 120°C and (b) subsequent recovery above Tg. Bar is 1 mm.



Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US04/037510

International filing date: 08 November 2004 (08.11.2004)

Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/517,853
Filing date: 06 November 2003 (06.11.2003)

Date of receipt at the International Bureau: 20 December 2004 (20.12.2004)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)

World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse